Transcriptional Regulation of Retinal Fate Determination from Human Induced Pluripotent Stem Cells

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Vertebrate eye development is a complex process that is dependent upon the activity of numerous transcription factors. However, the process by which a retinal fate is specified from a primitive anterior neural progenitor cell remains largely elusive. Human induced pluripotent stem cells (hiPSCs) allows for the unique ability to recapitulate events during human development at stages that would otherwise be inaccessible to investigation. Building upon our previous studies, we sought to establish the role of key transcription factors during the establishment of a retinal fate. hiPSCs were directed to differentiate toward a retinal lineage using a targeted, stepwise differentiation process that mimics human retinogenesis. Experiments were designed to assess the developmental stages at which retinal cell fate determination was established from a primitive anterior neural population. Samples were collected every two days over the first twenty days of differentiation and gene expression analysis was performed via qPCR and immunocytochemistry. From a primitive anterior neural population derived from hiPSCs, populations of retinal and forebrain progenitor cells could be readily identified within the first 20 days of differentiation. During this timecourse, retinal populations were characterized by the expression of key transcription factors which were absent from other non-retinal cell types. The effects of these candidate genes were determined via qPCR and immunocytochemistry analyses to establish their ability to specify an early retinal fate. The work presented in this study helps to elucidate the mechanisms by which a retinal fate is specified from a more primitive population. The results of this study will assist in the establishment of efficient methods to generate retinal cells from hiPSCs and help establish these cells as a unique *in* vitro model system for studies of human development.

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